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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/405,046

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MEADE

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EXAMINER

JONES, D

ART UNIT

PAPER NUMBER

1619

DATE MAILED:

05/11/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

**Office Action Summary**

Application No.

09/405,046

Applicant(s)

MEADE ET AL.

Examiner

D. L. Jones

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 05 March 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 2-5 and 8-23 is/are pending in the application.
- 4a) Of the above claim(s) 3-5, 8-10, 13-15, 20, and 21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2, 11, 12, 16-19, 22, and 23 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.

- 18) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: \_\_\_\_\_.

### **ACKNOWLEDGMENTS**

1. The Examiner acknowledges receipt of Paper No. 11, filed 3/5/01, wherein (1) the specification was amended; (2) claims 1, 6, and 7 were canceled; (3) claim 16 was amended; and (4) claims 20-23 were added.

**Note:** Claims 2-5 and 8-23 are pending.

### **APPLICANT'S INVENTION**

2. The instant invention is directed to MRI agents and methods of use thereof.

### **RESPONSE TO APPLICANT'S ARGUMENTS/COMMENTS**

3. The Applicant's arguments filed 3/5/01 (Paper No. 11) to the rejection of claims 1, 6, 7, and 12-19 made by the Examiner under 35 USC 103, 112, and/or double patenting have been fully considered and deemed persuasive for reasons of record in Applicant's response. Therefore, the said rejections are hereby withdrawn.

### **COMMENTS/NOTES**

4. It should be noted that the search was not extended beyond Applicant's elected species as set forth in Paper No. 7, filed 6/26/2000, because prior art was found to render the species obvious.

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## **WITHDRAWN CLAIMS**

5. Claims 3-5, 8-10, 13-15, 20, and 221 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention/species.

## **NEW GROUNDS OF REJECTION**

### **Double Patenting**

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

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7. Claims 2, 11, 16-19, 22, and 23 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 9, 11, 14, and 16 of U.S. Patent No. 5,707,605. Although the conflicting claims are not identical, they are not patentably distinct from each other because it would have been obvious to one of ordinary skill that R1-R12 may have all the values as set forth by Applicant with the exception of R1-R12 being aryl (see claim 2 (instant invention) and claim 11 (patent)). Likewise, it would have been obvious to select a peptide as a blocking agent in column 14, line 55, it is disclosed that a blocking agent may be a peptide or polypeptide. In addition, it would have been obvious to allow the bonds between the nitrogen groups to be either single bonds or double bonds because the patented invention discloses such possible combinations.

8. Claims 2, 11, 12, 16-19, 22, and 23 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 6, 9, 29, and 30 of U.S. Patent No. 5,980,862. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to MRI agents and methods thereof comprising a blocking agent. In particular, it would be obvious that the term 'blocking agent' encompasses peptides based on how Applicant has defined blocking agent in column 14, lines 1-12. In addition in column 13, lines 23-64, it is disclosed that 'blocking agent' also encompasses proteases such as caspase, interleukin-converting enzyme, cysteine protease, serine protease, calpain, cathepsine, and metalloproteinase.

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**112 Rejections**

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 11, 12, 16-19, 22, and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 11, 12, 16-19, 22, and 23: The claims as written are ambiguous because the claims depend upon canceled claims 1, 6, and or 7.

**103 Rejections**

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. Claims 2, 11, 12, 16, 17, 22, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garlich et al (US Patent No. 5,133,956) in view of Watson (US Patent No. 5,914,095).

**Garlich et al** disclose the radiolabeling of metal binding proteins. In addition, Garlich et al disclose (1) examples of possible bifunctional chelators that have a metal chelating moiety and a reactive group by which the compound is covalent coupled to a protein. Possible chelators include polyaminocarboxylates such as 1,4,7-tris-

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carboxymethethyl-1,4,7,10-tetraazacyclododecane (DOTA) and its analogs (column 3, lines 10-50). (2) Methods of generating the chelators are well known in the art. For example, one or more carboxylic acid groups of the polyamine, polycarboxylic acid chelator may be activated by conversion to activating groups such as internal or mixed anhydrides and activated esters (i.e. para-nitrophenyl). Next, the activated acid group is reacted with the protein and the metal ion is added to the protein chelator complex (column 4, lines 4-13). (3) The modification of the protein by the addition of chelators may be accomplished by methods known in the art. However, generally, the method involves the formation of a covalent linkage with an amino acid residue of the protein and a functional group of the chelator which is capable of binding the protein (column 4, lines 29-35). (4) Possible radionuclides useful with the invention of Garlich et al include gadolinium among many other metals (column 4, lines 47-53). (5) Generally, the bifunctional chelators are capable of binding one atom of metal cation and in general will bind one molecule of protein. However, it is possible for one protein molecule to bind more than one bifunctional chelator molecule (column 5, lines 18-28). While Garlich et al disclose the conjugation of a DOTA analog to a protein, the reference fails to specifically disclose the chelator in combination with a peptide.

**Watson** discloses DOTA residues conjugated to a site-specific macromolecule and a metal ion useful for diagnostic imaging and radiotherapy (see entire document, especially, abstract; column 4, lines 17-31). Depending upon the type of imaging desired, the metal will vary (column 5, lines 5-9; column 11, lines 34-45; column 14, lines 29-50). In addition, Watson discloses site-direct macromolecules that may be

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conjugated to the DOTA residues. The possible macromolecules include proteins and peptides (column 11, lines 46-52).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Garlich et al using the teachings of Watson and attach a peptide to the DOTA analog because (1) (Garlich et al) column 3, lines 10-51, disclose that possible bifunctional chelators (polyaminocarboxylates) that may be coupled to a protein include DOTA. (2) Garlich et al disclose that gadolinium is a possible radionuclide to use with their invention (column 4, line 53). (3) Garlich et al disclose that the attachment the protein chelator to one or more of the carboxylic acid groups of the polyamine, polycarboxylic acid chelator is common in the art (column 4, lines 4-13 and 29-35). (4) Watson discloses DOTA conjugates capable of being conjugated to a metal and site-directed macromolecule for MRI purposes. Hence, since, Watson discloses that both proteins and peptides are site-directed macromolecules, it would be obvious to one of ordinary skill in the art to replace the protein of Garlich et al with a peptides, Furthermore, since both references disclose DOTA analogs capable of being conjugated to a site-directed macromolecule such as a protein or peptide and attached to a metal for magnetic resonance imaging, the references may be considered to be within the same field of endeavor; thus, the references are combinable.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (703) 308-4640.




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The examiner can normally be reached on Mon.-Fri. (alternate Mon.), 6:45 a.m. - 4:15 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Diana Dudash can be reached on (703) 308- 2328. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.



D. L. Jones  
Primary Examiner  
Art Unit 1619

May 8, 2001